REMARKS

Claims 1, 12, 13 and 17-50 are currently pending in this application. Claims 18, 19, 29-31 and 41-49 stand withdrawn. Claims 1, 20, 21, 28 and 50 are currently amended herein. Claims 26, 27 and 32 are cancelled herein without prejudice or disclaimer as to the subject matter thereof. Claims 2-11 and 14-16 were previously cancelled without prejudice or disclaimer as to the subject matter thereof. Applicants respectfully reserve the right to prosecute the subject matter of the cancelled claims in one or more Continuation or Divisional applications. Applicants respectfully submit that no new matter is introduced into the specification by way of the instant claim amendments.

Rejections

35 U.S.C. § 112, 1st paragraph, Written Description

Claims 1, 17, 20-28, 32-40 and 50 were rejected under 35 U.S.C. § 112, 1st paragraph as allegedly failing to comply with the written description requirement.

Applicants respectfully disagree and traverse this rejection. Without acquiescing in the merits of the rejection, it is noted that for purposes of expediting prosecution Applicants have amended claims 1 and 20 herein to direct those claims to the subject matter of SEQ ID NO:5.

The Office Action states (in part) that "[t]he specification ... does not disclose the relevance of the treatment with the clinical outcome observed, i.e., how the composition or vaccine comprising the peptides treat or prevent cancer." *See* Office Action, page 5, lines 23-29.

Applicants respectfully disagree and submit that the specification provides adequate written description support for the claimed subject matter, as well as for the position that the claimed compositions are useful in treating cancer. For instance, Example 2 states that

> Spontaneous cytotoxic T-cell responses to survivin-derived MHC class I restricted T-cell epitopes were demonstrated in situ as well as ex vivo in breast cancer, leukemia, and melanoma patients. Moreover, survivin reactive T cells isolated by magnetic beads coated with MHC/peptide complexes were cytotoxic to HLA-matched tumours of different tissue types. Being a universal tumor

> antigen, survivin may serve as a widely applicable target for anti-cancer immunotherapy.

See specification, page 26, lines 22-27. It is noteworthy that the modified survivin peptide Sur1M2 (SEQ ID NO:5) was one of the peptides against which patients developed survivin peptide-specific T-lymphocyte responses in PBLs as measured by ELISPOT. This included patients suffering from melanoma, breast cancer and chronic lymphatic leukemia (CLL) as evidenced by Table 2 on page 29 of the specification as originally filed.

Applicants also note that Example 5 states that

> Five heavily pretreated stage IV melanoma patients were vaccinated with the modified HLA-A2-restricted survivin epitope, namely the sur1M2 peptide [SEQ ID NO:5], presented by autologous dendritic cells in a compassionate use setting. Four of the patients mounted strong T-cell response to this epitope as measured by ELISPOT assay. Furthermore, in situ peptide/HLA-A2 multimer staining revealed the infiltration of survivin reactive cells into both visceral and soft tissue metastases. Notably, vaccination associated toxicity was not observed. The data demonstrate that it is feasible to induce T-cell response against survivin, even in late stage melanoma patients, and that these vaccinations are well tolerated.

See specification, page 44, lines 1-11.

In light of the instant amendments and remarks provided herein, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 17, 20-28, 32-40 and 50 under 35 U.S.C. § 112, 1st paragraph as allegedly failing to comply with the written description requirement. Applicants note that rejected claim 26, 27 and 32 are cancelled herein without prejudice or disclaimer.

35 U.S.C. § 112, 1st paragraph, Enablement

Claims 1, 17, 20-28, 32-40 and 50 were rejected under 35 U.S.C. § 112, 1st paragraph as allegedly failing to provide enablement commensurate with the scope of the claims.

Applicants respectfully disagree and traverse this rejection.

It is well established under 35 U.S.C. §112 ¶ 1, that "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the

patent coupled with information known in the art without undue experimentation." (United States v. Telectronics, Inc., 857 F.2d 778, 785 (Fed. Cir. 1986)). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), MPEP § 2164.01.

The Office Action states that "[i]t is the Examiner's position that ... (2) Examples 2 and 5 do not disclose a clinical response for treatment or prevention using SEQ ID NO:5, and Example 5 discloses that a T cell response could be elicited when dendritic cells were pulsed with SEQ ID NO:5 and administered *in vivo* and T cell infiltration of metastases could be observed, and the instant rejection does not acknowledge enablement for SEQ ID NO:5 except for the peptide consisting of SEQ ID NO:5, kit thereof, HLA-A2/complex or multimer thereof, not for the vaccine, pharmaceutical composition or other compositions ... (4) Dr. Andersen confirms that the only firm proof that a peptide is a vaccine or pharmaceutical is administration in phase III clinical trials that have not been completed ..." *See* Office Action, page 14, line 34 extending to page 15, line 13.

Applicants respectfully disagree with the position set forth in the Office Action that the claimed subject matter directed to SEQ ID NO:5 should be so limited. Respectfully, Applicants submit that the Office Action appears to be requiring completed human clinical trials in order to satisfy the enablement (and by extension the utility) requirement. Applicants note that the Federal Circuit has stated that

> FDA approval is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

In re Brana, 34 USPQ2d 1437, 1442, 1443 (Fed. Cir. 1995). *See also* MPEP § 2107.03 (IV)(entitled "Human Clinical Data") (8th Ed., 6th Rev.).

Applicants submit that the specification provides at least three separate examples that are useful in guiding a skilled artisan to use the claimed invention. Example 1 presents an experiment in which cytotoxic T-lymphocyte (CTL) responses to survivin-derived peptide epitopes were evaluated using either patients suffering from a form of cancer or healthy individuals. In Example 1, which sets forth the methodology involved in the example, it is noted that SEQ ID NO: 1, SEQ ID NO:4 and SEQ ID NO:5 each provided binding to HLA-A2. It is noteworthy that the SEQ ID NO:4 and SEQ ID NO:5 "peptides bind with almost similar high affinity to HLA-A2 as the positive control." *See* Specification, page 25, lines 13-16.

Example 2 and Example 5 further evaluated responses to survivin-derived peptide epitopes. It is noted that for purposes of amended claim 1 that Example 2 and Example 5 evaluated SEQ ID NO:5.

As noted previously, regarding the Reker *et al* reference, Dr. Andersen explained that the "statement was presented in the discussion of the research data, not to express concerns with respect to the relevance of using survivin peptides in cancer immunotherapy, but merely to indicate that phase III clinical trials - the only firm proof that a vaccine works - had not yet been completed." *See* Declaration under 37 C.F.R. § 1.132 of Dr. Mads Hald Andersen, of record.

In light of the instant amendments and remarks provided herein, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 17, 20-28, 32-40 and 50 under 35 U.S.C. § 112, 1st paragraph. Applicants note that rejected claim 26, 27 and 32 are cancelled herein without prejudice or disclaimer.

35 U.S.C. § 112, 1st paragraph, Enablement

Claim 24 was rejected under 35 U.S.C. § 112, 1st paragraph as allegedly failing to comply with the enablement requirement. The Office Action asserts that there is insufficient disclosure in the specification on the breast cancer cell line MCF-7 and melanoma cell line FM3.

Applicants respectfully disagree and traverse.

Applicants submit that the breast cancer cell line MCF-7 is commercially available from the LGC Promochem / ATCC as ATCC Number HTB-22TM, and thus it is not an undue burden

on the skilled artisan to obtain this cell line. Regarding the melanoma cell line FM3, Dr. Andersen states in his declaration of record that "[t]he cell line was originally described by Kirkin et al (Cancer Immunol Immunother, 41:71-81 1995) and is well recognized within the art."

Applicants respectfully request reconsideration and withdrawal of the rejection of claim 24 under 35 U.S.C. § 112, 1st paragraph.

35 U.S.C. § 112, 2nd paragraph

a) Claim 20 was rejected as indefinite in the recitation of "[a] peptide ... comprising, for each specific HLA allele, any of the amino acid residues as indicated in the following table ..." Applicants submit that this rejection has been rendered moot by way of claim amendment, and respectfully request reconsideration and withdrawal of the rejection of claim 20 as indefinite.

b) Claim 24 was rejected as indefinite in the recitation of "... the breast cancer cell line MCF-7 and the melanoma cell line FM3." Applicants submit that the recitation of breast cancer cell line MCF-7 and melanoma cell line FM3 is not indefinite, as these are art recognized cell lines. For example, breast cancer cell line MCF-7 is commercially available from the LGC Promochem / ATCC as ATCC Number HTB-22TM. (*See* http://www.lgcpromochem-atcc.com/common/catalog/numSearch/numResults.cfm?atccNum=HTB-22). Regarding the melanoma cell line FM3, Dr. Andersen states in his declaration that "[t]he cell line was originally described by Kirkin et al (Cancer Immunol Immunother, 41:71-81 1995) and is well recognized within the art."

Prior Art Rejections

As an initial matter, Applicants respectfully address the characterization of both of the cited Andersen references as prior art. Applicants submit that the earliest priority filing (U.S.

provisional patent application no. 60/352,284) was filed on January 30, 2002, and includes disclosure of at least SEQ ID NO:5, to which amended claim 1 is now directed.

Applicants further submit that both Andersen references were published less than one year prior to the filing of Applicants' provisional patent application, for the reasons of record previously presented by Applicants. Because Applicants' provisional application was filed less than one year after the publication of the two Andersen references, Applicants submit that the Andersen references are not prior art under 35 U.S.C. § 102(b).

Furthermore, Applicants have previously submitted a declaration under 37 C.F.R. § 1.132 by inventor Mads Hald Andersen (of record), in which Dr. Andersen sets forth the contribution of each of the non-inventor and inventor authors of the two cited Andersen publications. Applicants submit that the declaration of Dr. Andersen establishes that the cited Andersen *et al* articles are describing Applicants' own work.

35 U.S.C. § 102 (b)

a) Claims 1, 17, 20-24, 36 and 38-40 were rejected under 35 U.S.C. § 102 (b), as allegedly anticipated by the disclosure of Andersen *et al* (Cancer Res., 2000, 61:869-872) as evidenced by Andersen *et al* (Cancer Res., 2001, 61:5964-5968).

Applicants respectfully disagree and traverse this rejection.

As discussed above, Applicants believe that neither of the cited Andersen *et al* references is prior art under 35 U.S.C. § 102 (b) to the claimed invention for the reasons provided. Furthermore, Applicants submit that the declaration of Dr. Andersen under 37 C.F.R. § 1.132 establishes that the Andersen *et al* articles are describing Applicants' own work. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 17, 20-24, 36 and 38-40 under 35 U.S.C. § 102 (b).

b) Claims 1, 17, 20-24, 36 and 38-40 were rejected under 35 U.S.C. § 102 (b), as allegedly anticipated by the disclosure of Andersen *et al* (Cancer Res., 2001, 61:5964-5968).

Applicants respectfully disagree and traverse this rejection.

As discussed above, Applicants believe that neither of the cited Andersen *et al* references is prior art under 35 U.S.C. § 102 (b) to the claimed invention for the reasons provided. Furthermore, Applicants submit that the declaration of Dr. Andersen under 37 C.F.R. § 1.132 establishes that the Andersen *et al* article is describing Applicants' own work. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 17, 20-24, 36 and 38-40 under 35 U.S.C. § 102 (b).

c) Claims 1, 17, 20-24, 36 and 38-40 were rejected under 35 U.S.C. § 102 (b), as allegedly anticipated by the disclosure of U.S. Patent No. 6,346,389, for the alleged disclosure of a subsequence corresponding to SEQ ID NO:14.

Applicants respectfully disagree and traverse this rejection.

As stated in MPEP § 2131, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Applicants submit that the disclosure of U.S. Patent No. 6,346,389 fails to teach all of the claimed elements. For example, U.S. Patent No. 6,346,389 fails to teach SEQ ID NO:5. As noted previously, Applicants submit that the declaration of Dr. Andersen under 37 C.F.R. § 1.132 establishes that the Andersen *et al* article is describing Applicants' own work. As U.S. Patent No. 6,346,389 does not teach all of the elements of the rejected claims as amended herein, U.S. Patent No. 6,346,389 does not anticipate the subject matter of the rejected claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 17, 20-24, 36 and 38-40 under 35 U.S.C. § 102 (b).

d) Claims 1, 17, 20-24, 36 and 38-40 were rejected under 35 U.S.C. § 102 (e), as allegedly anticipated by the disclosure of U.S. Patent No. 6,346,389, for the alleged disclosure of a subsequence corresponding to SEQ ID NO:14.

Applicants respectfully disagree and traverse this rejection.

As stated in MPEP § 2131, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art

reference." Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Applicants submit that the disclosure of U.S. Patent No. 6,346,389 fails to teach all of the claimed elements. For example, U.S. Patent No. 6,346,389 fails to teach SEQ ID NO:5. As noted previously, Applicants submit that the declaration of Dr. Andersen under 37 C.F.R. § 1.132 establishes that the Andersen *et al* article is describing Applicants' own work. As U.S. Patent No. 6,346,389 does not teach all of the elements of the rejected claims as amended herein, U.S. Patent No. 6,346,389 does not anticipate the subject matter of the rejected claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 17, 20-24, 36 and 38-40 under 35 U.S.C. § 102 (e).

35 U.S.C. § 103(a)

a) Claims 1, 17, 20-25, 28 and 32-37 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over WO 00/03693 in view of Rammensee *et al.*, Ruppert *et al.*, Conway *et al.* and U.S. Patent No. 6,572,864.

Applicants respectfully disagree and traverse this rejection.

According to the Office Action, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention in light of WO 00/03693, Conway *et al.*, Rammensee *et al.* and Ruppert *et al.* "in order to produce the nonamer peptide sequence FLKLDRERA (SEQ ID NO:1) and the nonamer subsequence STFKNWPFL (SEQ ID NO:14)." *See* Office Action, page 22, lines 15-22. The currently amended claims are not directed to SEQ ID NO:1 or SEQ ID NO:14. Applicants respectfully submit that the amended claims are not obvious in light of the disclosures of WO 00/03693, Conway *et al.*, Rammensee *et al.*, Ruppert *et al.* and US Patent No. 6,572,864. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 17, 20-25, 28 and 32-37 under 35 U.S.C. § 103(a).

b) Claims 38-40 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over WO 00/03693 in view of Rammensee *et al.*, Ruppert *et al.*, Conway *et al.*, U.S. Patent No. 6,572,864, and further in view of WO 99/50637.

Applicants respectfully disagree and traverse this rejection.

Claims 38-40 ultimately depend from and incorporate the elements of claim 1. Applicants submit that claim 1 is not rendered obvious by these references for the reasons set forth above. Applicants respectfully submit that claims 38-40 are also not obvious for at least the reasons set forth above with respect to claims 1, 17, 20-25, 28 and 32-37. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 38-40 under 35 U.S.C. § 103(a).

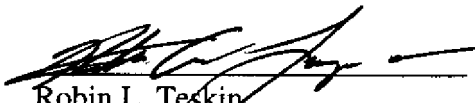
CONCLUSION

An indication of allowance of all claims is respectfully solicited. Early notification of a favorable consideration is respectfully requested.

Respectfully submitted,

HUNTON & WILLIAMS LLP

Date: June 12, 2008

By: 

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